Brief Description of the Drawings

-- Figure 11 shows SEM images of a sample of fenofibrate processed by the method of the invention at 50 ° C and 190 bar at

a) 100 x magnification and

b) 3510 x magnification.

Figure 12 shows SEM images of gemfibrozil processed by the method of the invention using CO_2 at a pressure of 190 bar and temperatures of

a) 50 ° C and

b) 25 ° C.—

In the Claims

Please delete claims 2, 11, 15, 19, 25 and 34. New claims 39-41 have been added. Please amend claims 3, 4, 6, 8-10, 12-14, 16-18, 20-22, 24, 26-27, 29-31, 35-36 and 38 as set forth below.

Listing of Claims:

Please enter the following rewritten claims:

1. (Original) A method for manipulating or formulating a solid substance which melts under pressure of a gas without degrading at a temperature which is lower than the melting point of the substance at atmospheric pressure including:

applying to the substance a liquefied gas or dense gas to melt the substance without degrading the substance;

then contacting the molten substance with a carrier fluid, which is at substantially the same pressure as the liquefied gas or dense gas, to form a solution or mixture of at least a part of the molten substance and the carrier fluid; and

passing the solution or mixture into a vessel of lower pressure than the pressure of the liquefied gas or dense gas and carrier fluid to form particles of the substance.

2. (Cancelled)

3. (Currently Amended) A method according to claim 1 ~~or claim 2~~, wherein the carrier fluid is the same as the liquefied gas or dense gas.

4. (Currently Amended) A method according to ~~any one of~~ claims 1 ~~to 3~~ further including allowing the substance and the liquefied gas or dense gas to equilibrate for at least one minute before the contacting step.

5. (Original) A method according to 4, wherein the equilibration step is for a period of about 2 hours.

6. (Currently Amended) A method according to ~~any one of~~ claims 1 ~~to 5~~, wherein the substance is a pharmaceutical or biological compound.

7. (Original) A method according to claim 6 wherein the substance is cyclosporine.

8. (Currently Amended) A method according to ~~any one of~~ claims 1 ~~to 7~~, wherein the temperature is between 5°C and 150°C.

9. (Currently Amended) A method according to ~~any one of~~ claims 1 ~~to 8~~, wherein the pressure of the liquefied gas or dense gas and carrier gas is between 5 bar and 200 bar.

10. (Currently Amended) A method according to ~~any one of~~ claims ~~1 to~~ 9 wherein the liquefied gas or dense gas is carbon dioxide.

11. (Cancelled)

12. (Currently Amended) A method according to ~~any one of~~ claims 1 ~~to 11~~, wherein at least 50% of the particles formed are between 50 and 5000 nanometers in diameter.

13. (Currently Amended) A method according to ~~any one of~~ claims 1 ~~to 12~~, wherein over 50% of the particles are less than 5000 nanometers in diameter.

14. (Currently Amended) A method according to ~~any one of~~ claims 1 ~~to 13~~, wherein the particles are encapsulated, the method further including the addition of an encapsulating material <u>after the passing of the solution or mixture into a vessel of lower pressure</u>.

15. (Cancelled)

16. (Currently Amended) A method according to claim 14 ~~15~~ wherein the encapsulating material is biodegradable.

17. (Currently Amended) A method according to ~~any one of~~ claims 14 ~~to~~ ~~16~~, wherein the encapsulating material is selected from the group consisting of polyethylene glycol, polyvinylpyrrolidone, poly(d,l-lactide-co-glycolide), poly cellulose acetate.

18. (Currently Amended) A method according to ~~any one of~~ claims 14 ~~to~~ ~~17~~, wherein the encapsulated particles contain a mixture or combination of the substance and the polymer for sustained release applications.

19. (Cancelled)

20. (Currently Amended) Particles of a substance formed by a method according to ~~any one of the previous~~ claims 1.

21. (Currently Amended) Encapsulated particles of a substance formed by a method according to ~~any one of~~ claims 13 ~~14 to 19~~.

22. (Currently Amended) Particles according to ~~any one of~~ claims 20 ~~or~~ ~~claim 21~~, wherein the particles include a pharmaceutical or biological substance.

23. (Original) Particles according to claim 22 wherein the particles include primarily cyclosporine.

24. (Currently Amended) Particles according to ~~any one of~~ claims 20 ~~to 23~~, wherein at least 50% of the particles are between 50 and 5000 nanometers in diameter.

25. (Cancelled)

26. (Currently Amended) A composition suitable for aerosol delivery including particles formed by a method according to ~~any one of~~ claims 1 ~~to 19~~.

27. (Currently Amended) A method of treatment of a subject including administering to the subject an effective amount of fine particles of a substance produced by a method according to ~~any one of~~ claims 1 ~~to 19~~.

28. (Original) A method according to claim 27 wherein the substance is a pharmaceutical or biological compound.

29. (Currently Amended) A method according to claim 27 ~~or claim 28~~ wherein the administration of the substance is by inhalation.

30. (Currently Amended) A method according to claim 24 ~~27 or claim 28~~ wherein the administration is by transdermal application, oral, controlled or sustained release.

31. (Currently Amended) An apparatus for producing particles by the method according to ~~any one of~~ claims 1 ~~to 19~~, including:

a pressure chamber having an inlet and an outlet, the outlet being above the inlet;

a first conduit means connected to the inlet for supplying the liquefied gas or dense gas to the pressure chamber; and

a second conduit means extending from the outlet to a depressurisation point.

32. (Original) An apparatus according to claim 31, further including flow control means to control flow along the second conduit means.

33. (Original) An apparatus according to claim 32, further including a third conduit means connected to the downstream end of the second conduit means downstream of the flow control means for supplying liquefied gas or dense gas, or carrier fluid, at pressure to the depressurisation point.

34. (Cancelled)

35. (Currently Amended) An apparatus according to ~~any one of~~ claims 33 ~~31 to 34~~, wherein the apparatus upstream of the depressurisation point is maintained at a constant temperature by a temperature bath.

36. (Currently Amended) A pharmaceutical composition including particles of a substance produced by a method according to ~~any one of~~ claims 1 ~~to 19~~.

37. (Original) A pharmaceutical composition according to claim 36, wherein the substance is a pharmaceutical or biological compound.

38. (Original) A pharmaceutical composition according to claim 36 ~~37~~, wherein the substance is cyclosporine.

Please add the following new claims:

39. (New) A method according to claim 6 wherein the substance is gemfibrozil or fenofibrate.

40. (New) Particles according to claim 20 wherein the particles include primarily gemfibrozil or fenofibrate.

41. (New) A pharmaceutical composition according to claim 36, wherein the substance is gemfibrozil or fenofibrate.